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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,609	04/25/2001	Vitaliy Arkadyevich Livshits	206339US0	4787

22850 7590 03/10/2003

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/841,609	LIVSHITS ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 6, mailed on September 23, 2002), Applicants filed an election received on January 10, 2003 (Paper No. 9). Claims 1-8 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group II, Claims 4-7, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that no adequate reasons and/or examples have been provided to support a conclusion of patentably distinctness between the identified groups and that no search burden would be required to search all the claims together. This is not found persuasive because the distinctness of Groups I and II was previously noted by virtue of their distinct structures – *Escherichia* with sucrose PTS genes and *Escherichia* with sucrose non-PTS gene have distinct structures (containing distinct genes) whose searches would not be co-extensive. Group III was also described as distinct by virtue of the product and process of use analysis previously presented with respect to Groups I and II. Group III could be rejoined if Group II is found allowable as previously noted.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-8 are pending. Claims 1-3 and 8 are withdrawn from further consideration as non-elected inventions. Claims 4-7 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the foreign application 2000110350 filed on April 26, 2000 in Russia as requested in the declaration. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. Said papers are not in English; a translation would be required if the priority date is necessary for purposes of prior art.

Information Disclosure Statement

4. The information disclosure statements filed on October 31, 2001 (Paper No. 3), December 3, 2001 (Paper No. 4), and March 12, 2002 (Paper No. 5) have been reviewed, and their references have been considered as shown by the Examiner's initials next to each citation on the attached copies.

Objections to the Specification

5. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---*Escherichia* bacteria with non-PTS Genes for the Production of Amino Acids---

6. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the definition of the abbreviation "PTS" for clarity.

Objections to the Claims

7. Claim 4 is objected to for a typographical error; in line 2, the term "sucorse" should be --- sucrose---. Correction is required.

8. Claim 7 is objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim (Claim 6 is a multiple dependent claim). See M.P.E.P. § 608.01(n). Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 4-7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "sucrose non-PTS genes" in Claim 4 and the term "proton symport transport system" in Claim 5 are confusing as to the nature of the genes being introduced. The specification described sucrose non-PTS genes by way of example from Bockmann *et al.* (see page 4). In Bockmann *et al.*, a csc regulon is described encompassing cscB (a permease), cscK (a fructokinase), cscA (an invertase), and cscR (a repressor) (see Fig. 2). Must this exact regulon be used? If not, then what characteristics must a permease (or invertase or fructokinase or repressor) have to be considered useful in the sucrose non-PTS system? The exact nature of sucrose non-PTS genes is wholly unclear. Moreover, does the term "proton symport transport system" mean the permease described by Bockmann *et al.*? If so, why the different name? Clarification is required so that the metes and bounds of the instant claims can be determined.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to bacterium transformed with a gene that is claimed solely by function and without any structural limitations wherein the functions described do not adequately support the genus claimed.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, the use of the csc regulon from Bockmann *et al.* comprising a permease, a fructokinase, an invertase, and a repressor in *E. coli* to promote sucrose utilization is described. No description of how these enzymes, working together, promote sucrose utilization is offered so that one of skill in the art would be able to identify other permease, fructokinase, invertase, and or repressor genes that could functionally substitute for those described by Bockmann *et al.*. No generic structure is provided. No particular functionality is provided, i.e., not *every* proton symport transport system (permease) will be effect in sucrose utilization. For these reasons, the breadth of the instant claims is not adequately described in the instant specification as filed.

11. Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for *Escherichia* bacteria harboring the csc regulon (four genes) described in the specification and in Bockmann *et al.*, does not reasonably provide enablement for *Escherichia* bacteria harboring any non-PTS gene set. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make the claimed bacteria to the extent required by the scope of the instant claims would required undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The specification provides a single example of non-PTS genes, as a set, and use of these genes in two examples, Example 5 to produce isoleucine and Example 8 to produce tryptophan. No guidance or examples of non-PTS genes other than those described by Bockmann *et al.* is described. No description of how the Bockmann *et al.* genes work to promote sucrose utilization is offered to disclose to one of skill in the art how to choose other regulons as non-PTS genes. The state of the prior art describes only this one regulon in Bockmann *et al.* It is wholly unpredictable if another non-PTS regulon exists. Thus, the instant claims are not enabled to the full extent of their scope.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claim 1, as written, does not sufficiently distinguish over cells as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated". Alternatively, the Examiner suggests requiring the non-PTS gene to be on a heterologous plasmid and harbored by the bacterium. See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Bockmann *et al.* (see IDS). The instant claims are drawn to *E. coli* harboring the non-PTS genes as described on page 4 of the instant specification – a permease, a fructokinase, an invertase, and a repressor as described in Bockmann *et al.*

In one aspect, the *E. coli* strain EC3132, a wild-type isolate that harbors the csc regulon (a permease, a fructokinase, an invertase, and a repressor) in its genome taught by Bockmann *et al.*, anticipates the instant claims. Nowhere in the instant claims is there a distinction between

naturally occurring bacteria and non-naturally-occurring sucrose-utilizing *E. coli* strains. The phrase "which has been constructed from a sucrose non-assimilative strain" carries little patentably weight in a product claim since it represents the precursor of the product; only if this precursor helps define the end product that is claimed does such a phrase add limitation. In this case, EC3132 does not differ from a K12 strain wherein the csc regulon as been incorporated into the genome by homologous recombination. Thus, EC3132 itself, as taught by Bockmann *et al.*, anticipates the instant claims.

In a second aspect, on page 27 of Bockmann *et al.*, the transformation of *E. coli* JM109 with pJBL102 is taught. pJMBL102 contains the entire csc regulon (non-PTS genes) as shown in Figure 2 of Bockmann *et al.* Thus, JM109/pJMBL102 clearly anticipates the instant claims.

Conclusion

14. Claims 4-7 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
March 6, 2003